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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/529,273	03/25/2005	Gautam Vinod Daftary	24439.US	2139

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EXAMINER	
STONE, CHRISTOPHER R	
ART UNIT	PAPER NUMBER
4173	

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12/04/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/529,273	DAFTARY ET AL.	
	Examiner	Art Unit	
	Christopher R. Stone	4173	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/9/2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27, 29-50 and 52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27, 29-50 and 52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed November 20, 2007, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 27, 29, 31-50 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over (Cserati and Hollo) in view of (Links and Lewis).

Cserati and Hollo discloses a composition comprising cyclophosphamide (cytoxan), hydroxypropyl-β-cyclodextrin, and water (p.70, 1st column, lines 28-34, 2nd column, lines 3-6.) Cserati and Hollo further discloses that cyclodextrins increases the stability of guest molecules (p. 70, 1st column, line 4 and 5 and p.71, Table 1, Number 16.) Cserati and Hollo does not disclose the aforementioned composition further comprising mesna. Links and Lewis discloses that mesna is a commonly used chemoprotective agent in patients receiving ifosfamide and cyclophosphamide (p.305, 2nd column, lines 1-3.) Thus, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention, motivated by the desire to treat oxazaphosphorine-induced toxicity, to add mesna to the composition of cyclophosphamide, hydroxypropyl-β-cyclodextrin, and water thus resulting in the practice of the instantly claimed invention with a reasonable expectation of success. It also would have been obvious to a person of ordinary skill in the art at the time of the invention to prepare the composition by adding cyclophosphamide and mesna (as such or as an aqueous solution optionally containing a etherified β-cyclodextrin) to an aqueous solution of hydroxypropyl-β-cyclodextrin to maintain the stability of the compounds. Mixing and making up the volume with water would have been obvious to a person of ordinary skill in the art at the time of the invention as well.

The optimization of composition components would have been obvious to one of ordinary skill in the art at the time of the invention. Optimization of the molar substitution of Hydroxypropyl-β-cyclodextrin would have been desired to acquire favorable solubility and complex formation. Optimization of Hydroxypropyl-β-cyclodextrin content would

have been desired for optimal stability of the composition. Optimization of oxazaphosphorine concentration would have been desired for optimal therapeutic effect. Optimization of the oxazaphosphorine to mesna ratio would have been desired to ensure optimal therapeutic effect with minimal urotoxicity.

The addition of parenteral additives to the composition at any step in the preparation would have been obvious to one of ordinary skill in the art at the time of the invention. The addition of additives such as buffers, diluents and chelators would have been desired to adjust the pH, to maintain the pH, to adjust the volume, to adjust the concentration, and to further increase stability.

Filter sterilizing the composition, aseptically filling it into sterile containers and sealing the containers would have been obvious to one of ordinary skill in the art at the time of the invention. Sterility would have been desired to avoid infection caused by contaminants in the composition. Using filter sterilization would have been particularly desirable since other sterilization techniques involve heating, which may deteriorate composition components.

Ifosfamide and cyclophosphamide were commonly used cancer drugs at the time of the invention. Therefore it would have been obvious to one of ordinary skill at the time of the invention to use the instantly claimed composition to treat a malignant disease because the therapeutically active oxazaphosphorine compounds were already commonly used for this purpose.

Claim 27 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over (Cserati and Hollo), in view of (Links and Lewis) and (Baumann and Preiss).

Cserati and Hollo and Links and Lewis disclose the aforementioned inventions, but they do not disclose the composition of the instantly claimed invention comprising ifosfamide. However, the composition of the instantly claimed invention comprising the oxazaphosphorine compound cyclophosphamide is disclosed. Baumann and Preiss discloses that cyclophosphamide and ifosfamide are the two most commonly used oxazaphosphorine compounds (p. 174, 1st column, lines 7-8.) The two compounds are isomers and share a very similar structure. Thus it would have been obvious to one of ordinary skill in the art at the time of the instant invention to use either oxazaphosphorine compound (cyclophosphamide or ifosfamide) in the composition of Cserati and Hollo and to add mesna, since both compounds cause bladder toxicity. Thus resulting in the practice of the claimed invention with a reasonable expectation of success.

Note: Claim 52 was inadvertently not included in the heading of the rejection under 35 U.S.C. 103(a) in the non-final rejection dated August 7, 2007; however the limitations of claim 52 were addressed in the body of the rejection (p. 7). Therefore this rejection does not constitute a new ground of rejection; the addition of claim 52 is merely correcting a typographical error.

Applicant argues that Cserati discloses complexation of some 23 cancer drugs with HPBCD, but does not include oxazaphosphorines and therefore complexing an oxazaphosphorine with HPBCD would not have been obvious to one of ordinary skill in the art at the time of the instantly claimed invention. This is not found persuasive because Cserati does disclose the complexation of the oxazaphosphorine,

cyclophosphamide (cytoxan) with HPBCD, as mentioned above (see p.70, 1st column, lines 28-34, 2nd column, lines 3-6 and p.71, Table 1, Number 16, cytoxan). Applicants further argue that there is no motivation in Cserati or Links and Lewis to add mesna to the composition of HPBCD and cyclophosphamide. This is not found persuasive because cyclophosphamide and mesna were known in the art to be administered together, as previously made of record (Links and Lewis, p.305, 2nd column, lines 1-3.) Therefore it would have been obvious for one of ordinary skill in the art at the time of the instantly claimed invention to combine mesna and the composition of HPBCD and cyclophosphamide to administer them together. Applicant is reminded of In re Burhans, 154 F.2d 690, 69 USPQ330 (CCPA 1946) which affirmed that selection of any order of performing process steps (e.g. administering the mesna and cyclosphosphamide sequentially or combining the compounds into a composition prior to administration) is prima facie obvious in the absence of new or unexpected results.

Conclusion

Claims 27, 29-50 and 52 are rejected. No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher R. Stone whose telephone number is (571) 270-3494. The examiner can normally be reached on Monday-Thursday, 7:30am-4:00pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

29November2007
CRS

/Cecilia Tsang/
Supervisory Patent Examiner, Art Unit 4173